=> d ibib abs 104
4 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):1-4

L11 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60122 CAPLUS
DOCUMENT NUMBER: 140:123179
TITLE: Methods for the production and therapeutic uses of VEGF traps made from **Ig domains** of VEGF receptors 1, 2 and 3
INVENTOR(S): Daly, Thomas J.; Fandl, James P.; Papadopoulos, Nicholas J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 9,852.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014667	A1	20040122	US 2003-609775	20030630
WO 2000075319	A1	20001214	WO 2000-US14142	20000523

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1999-138133P P 19990608
WO 2000-US14142 W 20000523
US 2001-9852 A2 20011206

AB Nucleic acid mols. and multimeric proteins capable of binding vascular endothelial growth factor (VEGF). VEGF mini-traps are disclosed which are therapeutically useful for treating VEGF-associated conditions and diseases, and are specifically designed for local administration to specific organs, tissues, and/or cells.

L11 ANSWER 2 OF 4 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:708718 SCISEARCH
THE GENUINE ARTICLE: 235AH
TITLE: Characterization of the VEGF binding site on the Flt-1 receptor
AUTHOR: Herley M T; Yu Y; Whitney R G; Sato J D (Reprint)
CORPORATE SOURCE: AMER TYPE CULTURE COLLECT, DIV CELL MOL & DEV BIOL, 10801 UNIV BLVD, MANASSAS, VA 20110 (Reprint); AMER TYPE CULTURE COLLECT, DIV CELL MOL & DEV BIOL, MANASSAS, VA 20110; ST JUDE CHILDRENS HOSP, DEPT BIOCHEM, MEMPHIS, TN 38105; CHILDRENS HOSP, SURG RES LAB, BOSTON, MA 02115
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (7 SEP 1999) Vol. 262, No. 3, pp. 731-738.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0006-291X.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The angiogenic growth factor VEGF binds to the receptor tyrosine kinases **Flt-1** and **KDR/Flt-1**. **Immunoglobulin** (**Ig**)-like loop-2 of **Flt-1** is involved in binding VEGF, but the contribution of other **Flt-1 Ig**-loops to VEGF binding remains unclear. We tested the ability of membrane-bound **chimeras** between the extracellular **domain** of **Flt-1** and the cell adhesion molecule embigin to bind VEGF. VEGF bound as well to receptors containing **Flt-1** loops 1-2 or 2-3 as it did to the entire **Flt-1** extracellular **domain.** **Chimeras** containing only loop-2 of **Flt-1** bound VEGF with 22-fold lower affinity. We conclude that high-affinity VEGF binding requires **Ig**-like loop-2 plus either loop-1 or loop-3. In addition, **Flt-1** amino acid residues Arg-224 and Asp-231 were not essential for high-affinity binding of VEGF to membrane-bound **Flt-1.** (C) 1999 Academic Press.

L11 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:776257 CAPLUS
DOCUMENT NUMBER: 128:47303
TITLE: Chimeric forms of vascular endothelial growth factor receptor proteins as novel inhibitors of vascular endothelial growth factor activity
INVENTOR(S): Davis-Smyth, Terri Lynn; Chen, Helen Hsifei; Presta, Leonard; Ferrara, Napoleone
PATENT ASSIGNEE(S): Genentech, Inc., USA; Davis-Smyth, Terri Lynn; Chen, Helen Hsifei; Presta, Leonard; Ferrara, Napoleone
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744453	A1	19971127	WO 1997-US7694	19970506
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6100071	A	20000808	US 1996-643839	19960507
CA 2253738	AA	19971127	CA 1997-2253738	19970506
AU 9730604	A1	19971209	AU 1997-30604	19970506
AU 717112	B2	20000316		
EP 907733	A1	19990414	EP 1997-925475	19970506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000502357	T2	20000229	JP 1997-542429	19970506
JP 3457330	B2	20031014		
US 5952199	A	19990914	US 1997-874678	19970613
US 6383486	B1	20020507	US 1999-348886	19990701
US 2003092604	A1	20030515	US 2002-105901	20020320

PRIORITY APPLN. INFO.: US 1996-643839 A 19960507
WO 1997-US7694 W 19970506
US 1999-348886 A1 19990701

AB The present invention is directed to novel **chimeric** VEGF receptor proteins comprising amino acid sequences derived from the vascular endothelial growth factor (VEGF) receptors **flt-1** and **KDR**, including the murine homolog to the human **KDR** receptor **FLK-1**, wherein said **chimeric** VEGF receptor proteins bind to VEGF and antagonize the endothelial cell proliferative and angiogenic activity thereof. The present invention is also directed to nucleic acids and expression vectors encoding these **chimeric** VEGF receptor proteins, host cells harboring such expression vectors, pharmaceutically acceptable compns. comprising such proteins, methods of preparing such proteins and to methods utilizing such proteins for the treatment of conditions associated with undesired vascularization. Thus, the amino acid sequences of the extracellular ligand-binding **region** of **flt-1**, **KDR**, and **FLT4** receptors were aligned and the boundaries of each of the seven **Ig**-like **domains** were determined An **flt-1**/IgG (immunoadhesin) construct is then constructed and utilized as a template to systematically delete each of the 7 individual **Ig**-like **domains** of the **flt-1** extracellular ligand-binding **region** by employing the loop-out mutagenesis technique, while also creating unique restriction sites at the boundaries to be used for inserting other **Ig**-like **domains** obtained from other VEGF receptor ligand-binding **regions.** The **Ig**-like **domain** 2 of the **flt-1** extracellular ligand-binding **region** is shown to be required for specific binding to the VEGF ligand but in insufficient by itself to allow binding; the ability to bind VEGF was completely restored when **Ig**-like **domains** 1, 2, and 3 were all 3 present in combination. **Replacing** the **flt-1 Ig**-like **domain** 2 with the **Ig**-like **domain** 2 of the **KDR** receptor functions to establish the ability to specifically bind to the VEGF ligand, whereas the presence of **FLT4 Ig**-like **domain** 2 did not establish binding ability. Each of the other **swap chimeras** constructed behaved similar to the wild-type **flt-1** receptor. The **flt-1**(2)/**FLT4** and the **flt-1**(1,2,3)/**FLT4 chimeric** receptors are able to bind and specifically respond to VEGF.

L11 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 97045100 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8890165
TITLE: The second immunoglobulin-like domain of the VEGF tyrosine kinase receptor Flt-1 determines ligand binding and may initiate a signal transduction cascade.
AUTHOR: Davis-Smyth T; Chen H; Park J; Presta L G; Ferrara N
CORPORATE SOURCE: Department of Cardiovascular Research, Genentech Inc., South San Francisco, CA 94080, USA.
SOURCE: EMBO journal, (1996 Sep 16) 15 (18) 4919-27.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19961210

AB Vascular endothelial growth factor (VEGF) is an angiogenic inducer that mediates its effects through two high affinity receptor tyrosine kinases, **Flt-1** and **KDR**. **Flt-1** is required for endothelial cell morphogenesis whereas **KDR** is involved primarily in mitogenesis. **Flt-1** has an alternative ligand, placenta growth factor (PlGF). Both **Flt-1** and **KDR** have seven **immunoglobulin** (**Ig**)-like **domains** in the extracellular **domain.** The significance and function of these domains for ligand binding and receptor activation are unknown. Here we show that deletion of the second domain of **Flt-1** completely abolishes the binding of VEGF. Introduction of the second domain of **KDR** into an **Flt-1** mutant lacking the homologous domain restored VEGF binding. However, the ligand specificity was characteristic of the **KDR** receptor. We then created **chimeric** receptors where the first three or just the second **Ig**-like **domains** of **Flt-1 replaced** the corresponding **domains** in **Flt-4**, a receptor that does not bind VEGF, and analyzed their ability to bind VEGF. Both **swaps** conferred upon **Flt-4** the ability to bind VEGF with an affinity nearly identical to that of wild-type **Flt-1.** Furthermore, transfected cells expressing these **chimeric** **Flt-4** receptors exhibited increased DNA synthesis in response to VEGF or PlGF. These results demonstrate that a single **Ig**-like **domain** is the major determinant for VEGF-PlGF interaction and that binding to this **domain** may initiate a signal transduction cascade.

=> d his

(FILE 'HOME' ENTERED AT 11:27:34 ON 20 NOV 2004)

FILE 'MEDLINE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 11:27:51 ON 20 NOV 2004

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L1        502778 S IG OR IMMUNOGLOBULIN
L2       7424739 S DOMAIN? OR REGION? OR PORTION? OR COMPONENT?
L3          5702 S FLT1 OR (FLT(W)1) OR VEGFR1 OR (VEGFR(W)1)
L4         10476 S FLK1 OR KDR OR VEGFR2 OR (FLK(W)1) OR (VEGFR(W)2)
L5          1625 S FLT4 OR VEGFR3 OR (FLT(W)4) OR (VEGFR(W)3)
L6       1750740 S SWAP? OR SWITCH? OR REPLAC? OR FUSION? OR CHIMERA? OR CHIMERI
L7         50046 S L1(S)L2
L8          3683 S L3(P)(L4 OR L5)
L9          7551 S L7(P)L6
L10            7 S L7 AND L8 AND L9
L11            4 DUP REM L10 (3 DUPLICATES REMOVED)
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